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(54) Title: MULTI-DIMENSIONAL CHROMATOGRAPHY SYSTEM FOR PROTEOMICS

(57) Abstract: The present invention relates to multidimensional chromatography systems for proteomics and methods for identifying lower-abundance proteins in body fluids. Abundant proteins(s) is first removed by affinity chromatography utilizing affinity chromatographic column functionalized with ligand capable of selectively binding the abundant protein in the sample. Multidimensional chromatographic techniques are applied to the eluent with a reduced content of the abundant protein followed by mass spectrometric analysis.



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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/25367

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 24/00, 33/00, 30/02, 33/566

US CL : 436/173, 86, 161, 501

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 436/173, 86, 161, 501

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
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## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ARNAUD et al. "Purification of proteins by subtraction affinity chromatography", Protides of the Biological Fluids, 1979, volume date 1978, v. 26, pp. 649-52, Abstract	1-16
Y	ZHANG et al. "Multiple Separations Facilitate Identification of Protein Variants by Mass Spectrometry", Proteomics 2001, v. 1, pp. 1001-1009, the whole document	1-16
Y	"MULTIDIMENSIONAL CHROMATOGRAPHY": <a href="http://www.chem.agilent.com/cag/prod/lc/Application-multi.pdf">http://www.chem.agilent.com/cag/prod/lc/Application-multi.pdf</a> , 18 July 2002 (18.07.2002)	1-16
Y	WOLTERS et al. "An Automated Multidimensional Protein Identification Technology for Shotgun Proteomics", Anal. Chem., 2001, v. 73, pp. 5683-5690, the whole document	1-16
Y	REGNIER et al. "Multidimensional Chromatography and the Signature Peptide Approach to Proteomics", LCGC, February 2001, vol. 19, No. 2, pages 200-213; <a href="http://www.chromatographyonline.com">www.chromatographyonline.com</a> ; the whole document	1-16
X,P	ADKINS et al. "Toward a Human Blood Serum Proteome", Mol. Cell. Proteomics, 1.12, <a href="http://www.mcponline.org">http://www.mcponline.org</a> , 13 November 2002 (11.13.2002), the whole text	1-16
X,P	FERGUSON et al. "Proteome Analysis by Mass Spectrometry", Annu. Rev. Biophys. Struct., 24 January 2003, 32, pp. 399-424	1-16

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:	
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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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PCT/US03/25367

**Continuation of B. FIELDS SEARCHED Item 3:**

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isolation, purification, separation, proteins, polypeptides, peptides, "affinity chromatography", immunoaffinity, "size exclusion", proteomics, abundance